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Original Article

Clinico Pathological Study of Ovarian Tumors and its Relative Frequency in Women of Different Age Groups

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ABSTRACT

Introduction: Ovaries are common site for both benign and malignant tumors, the ovarian cancer being one of the major causes of suffering in women globally. They are seen in all age groups depending on their type. These tumors are responsible for major part of morbidity and mortality due to multitude of factors including socio-economic conditions, cultural issues and personal negligence. In order to diagnose these tumors just clinical and radiological findings are not sufficient; a thorough histopathological examination is the gold standard for ultimate diagnosis and management of patient.

Objectives: The main objective of this study is to evaluate clinic pathological features of benign and malignant ovarian tumors.

Material and Methods: This is a retrospective study of ovarian specimens that were received in the Histopathology section of Institute of Kidney Diseases (IKD) over a period 5 years from July 2014 till July 2019 from all the Gynecology Units of Hayatabad Medical Complex.

Results: A total of 229 cases of ovarian tumors were included in this study with age range from 1 year to 80 years. Maximum number of both benign and malignant tumors was seen in the age groups from 21-40years. Most common presentation was abdominal pain followed by abnormal uterine bleeding. 78.6% were married,64.19% cases were premenopausal, and 61% were nulliparous.63.31% cases were benign, 2.19% were borderline while 34.49% were malignant. Most common benign tumor was dermoid cysts followed by serous and mucinous cystadenoma. The most common malignant tumor was papillary serous cystadenocarcinoma.

Conclusions: The majority of ovarian tumors in our study were benign among which dermoid cyst was most frequent. Among malignant tumors the most frequent was papillary serous cystadenocarcinoma. Most common risk factors associated with ovarian tumors were nulli parity, menstrual irregularities, previous surgeries and a family history of ovarian/breast cancers.

Keywords: Benign, Malignant, Ovarian Carcinoma, Papillary serous cystadenocarcinom

Introduction

Globally cancer is considered to be a root cause of morbidity and mortality[1, 2]. Presently, it is a persistent barrier in achieving desirable life span in the majority of countries.[3]

Ovaries represent intra pelvic reproductive organs and are frequently affected by both benign and malignant tumors throughout life time from early years to menopause.[4] Due to the complex and diverse histogenesis of ovaries nearly any type of tumor can be seen but mostly ovarian tumors arise from four major components such as surface epithelium, germ cells, sex cord and stromal tissue.[5]

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Cancer of the ovaries is the fifth key source of cancer related mortality in females.[6]Due to vague symptoms of ovarian tumors, most patients are misdiagnosed as abdominal problems or menstrual disorders and therefore around 68 % are diagnosed at late stage resulting in lower survival rates and poor prognosis compared to those diagnosed at an earlier stages .[6] According to world statistics only 19 % of ovarian cancers are diagnosed at early stage resulting in poor response to treatment and higher mortality.[5,6]Histopathology of ovarian tumors is crucial for accurate diagnosis and management of patient.

The prevalence of carcinoma of the ovaries varies worldwide due to multiple risk factors in different regions of the globe.[7] According to various studies non-Hispanic white women are most commonly affected but due to the variations in access to diagnostic and management facilities the death rates

are highest among African women.[8, 9] It is estimated that by avoiding or diminishing risk factors we can trim down cancer cases to as much as 1/3 to 2/5 of total cancer cases.[3]

As reported by the American Cancer Society, roughly 90% of ovarian tumors are epithelial in origin. These are further classified into serous, mucinous, endometrioid, clear cell, and undifferentiated types on the basis of histological features.[10] Fewer than 2% of ovarian cancers are of germ-cell origin, which includes teratoma, dysgerminoma, endodermal sinus tumor, and choriocarcinoma based on histological variations. Lastly, ovarian stromal cell tumors include about 1% of ovarian cancers.[11, 12].

The various risk factors for ovarian malignancy include infertility, advanced age specially the postmenopausal women above 60 years, family history of ovarian or breast cancer and mutations in certain genes particularly BRCA1 and BRCA2[13, 14, 15]. Pelvic inflammatory diseases, endometriosis and certain benign cysts also serve as precursor lesion for malignant tumors.[16-18]Alcoholism and cigarette smoking is interrelated with high rate of ovarian tumors.[19, 20] ·Diet rich in cholesterol, obesity and reduced physical activity is linked with amplified risk of ovarian cancer.[20]Risk of germ cell ovarian cancer is elevated in those girls and adolescent women, the mothers of whom had taken hormones at some stage in their pregnancies, had increased body mass index or were teenagers at the time of pregnancy.[12] Certain factors lessen the risk of ovarian cancers such as increased parity, lactation, advanced age at child birth, tubal ligation and other contraceptive methods.[19]

Diagnosis of ovarian tumors is a challenge for both the Histopathologist and the surgeon due to its diverse histomorphological features. It is very crucial to diagnose these tumors at early stage in order to avoid complications. The routinely used investigation modalities such as history, examination, radiological survey and serum tumor marker studies are helpful but it is the biopsy and histopathology which is considered as a gold standard for ultimate diagnosis of ovarian tumors.[12]

Objective

1. To analyze the frequencies of different ovarian tumors according to age groups.
2. To study the associated clinical features in ovarian tumors.

Materials and Methods

This retrospective study was conducted in the Histopathology section of Institute of Kidney Diseases Peshawar (IKD) over a period 5 years from July 2014 till July 2019 from all the Gynecology Units of Hayatabad Medical Complex (HMC) which is a tertiary care hospital and receives cases from all regions of the province. After the approval of Institutional ethical board and proper written consent from the patients the study was carried out. The sample size was calculated by WHO formula with a prevalence of 13.6%, CI of 95% and margin of error of 5 %. The calculated sample size was 173. We instead included 229 cases in the study. In the present retrospective study, neoplastic ovarian lesions both benign and malignant obtained either from cystectomy or hysterectomy with bilateral or unilateral salpingophrectomy is included which made a total number of 229 cases. All the non-neoplastic and functional lesions of ovaries were excluded from this study. The specimens were checked for autolytic changes and then processed in the tissue processor, stained with Eosin and Hematoxylin(H&E) stain and examined by the same pathologist to avoid the inter observer error. The relevant data such as age, parity, family history, and clinical presentation, radiological and operative findings were recorded from patient's hospital admission sheets. All the data was entered in excel sheets and analyzed using SPSS version 21. In order to classify different tumors WHO classification of ovarian tumors 4th edition has been used.

Results

In the present study total of 229 cases of ovarian tumors were analyzed from July 2014 to July 2019. Out of these 145 (63.31%) cases were benign, 5 (2.19%) cases were borderline and 79 (34.49) cases were malignant in nature

In our study the age range of the patients varies from 1 to 80 years. The youngest patient was 3 years old while the maximum age in our study was 80 years. The cases were divided into 8 age groups with difference of 10 years between each group. The maximum number of both benign and malignant tumors (65 cases) was seen in the age groups from 21-30 years followed by 31-40 years age group (51 cases). The malignant tumors were distributed uniformly from early years to late menopause.

In present study most of the benign as well as malignant tumors were seen in women who were nulliparous while least number of both tumors was

seen in women with parity greater than 6 .Out of the total 229 cases 180 (78.6%) were married while 49 (21.39%) were unmarried. The age of menarche ranged from 10-16 years. A total of 147 (64.19%) cases were premenopausal while 82 (35.80%) cases were postmenopausal.

In our study the most common presentation was abdominal pain followed by abnormal uterine bleeding. The frequency of various types of presenting symptoms is shown in Table 1.

Table 1: Clinical presentation of study cases n=229

Clinical Presentation	No of cases	%
Pain abdomen and pelvis region	70	30.56%
Abnormal uterine bleeding	60	26.2%
Abdominal pain +mass	35	15.28%
Abdominopelvic mass	30	13.1%
Asymptomatic	24	10.48%
Postmenopausal bleeding	5	2.18%
Amenorrhea	5	2.18%

In this study most of the benign tumors ranged from 5-9 cm in size, while most malignant tumors were more than 10 cm in size .In our study the maximum numbers of tumors were surface epithelial type (139 cases). The other major bulk is formed by germ cell tumors of which 68 cases were of benign cystic teratoma while 7 cases were mixed germ cell tumors. Sex cord stromal tumors accounted for 9 cases. There were 4 cases of poorly differentiated carcinoma and 1 case was ofmetastatic carcinoma.

Table 2: Histological type of Tumors n=229

Histological Type	No of cases	%
Surface epithelial tumors	139	60.69%
Germ cell tumors	75	32.75%
Sex cord stromal tumors	9	3.93%
Poorly differentiated tumors	4	1.74%
Hemangiopericytoma	1	0.43%
Metastatic tumor	1	0.43%
Total	229	100%

Among benign tumors the most common tumor in our study was Dermoid cyst (68 cases) followed by serous cystadenoma (55 cases) and then mucinous cystadenoma (22 cases). In borderline tumors there were 3 cases of serous borderline tumor and 2 cases of mucinous borderline tumor. In malignant tumors most common was papillary serous cystadenocarcinoma (36 cases). There were 9 cases of sex cord stromal tumors and 8 cases of endometroid carcinoma. Mixed germ cell tumor comprised of 7 cases while 6 cases of mucinous cystadenocarcinoma

The exposure to various risk factors was recorded from patient's admission sheets. In our study 140 patients had history of previous surgeries either cystectomy, TAH with or without bilateral salpingophrectomy or removal of products of conception. The percentage of nulliparous patients was high as much as 61% (140 cases). Previous history of irregular menstrual cycle was seen in 130 cases while history of contraceptive use was noted in 100 cases in this study. There were 60 cases that showed history of previous tumors, 50 cases with infertility and 30 cases with family history of cancers. In our study 20 patients had previous history of endometriosis or pelvic inflammatory disease and only 10 patients had history of smoking as shown in Table 3.

Table 3: Frequency of various risk factors n=229

Risk Factor	No of cases	%
Nulliparity	140	61.13%
Previous surgery	140	61.13%
Irregular menses	130	56.76%
History of previous cancers	60	26.2%
Infertility	50	21.83%
Family history of cancer	30	13.1%
History of Endometriosis/PID	20	8.73%

Discussion

Cancer of the ovary is the most common malignancy of females associated with high mortality and morbidity rates due to late diagnosis. The clinical and histomorphological presentation of ovarian tumors is diverse and wide ranging. Ovarian tumors are a heterogeneous group of tumors consisting of epithelial, germ cell and sex cord stromal tumors. In each of the groups, their biological behavior varies from benign to borderline to extremely lethal malignant forms.[20]It is mandatory to arrive at early diagnosis by histopathological examination of biopsy to plan proper management of such patients in order to improve prognosis.[12].

In our study 63.31% cases were benign, 2.19% were borderline while (34.49%) were malignant in nature. This is with minor differences similar to studies carried out by Sheela Km et al[4], Gupta et al[20], Jha , Kula deepa et al[18], and Suhail et al[17] as shown in table-4.

Table 4:Frequency of tumors in different studies

Study	Benign (%)	Borderline (%)	Malignant (%)
Sheela Km et al	85	3.4	11.6
Gupta et al	72.9	4.1	22.9
Kula deepa et al	82.35	3.68	13.97
Suhail et al	74.8	1.6	23.4
Present study	63.31	2.19	34.49

Tumors of the ovary can occur at any age from infancy to old age. Early age at menarch and late menopause after the age of approximately 52 years is significantly associated with ovarian cancers. In our study the minimum age was 3 years with dermoid cyst while the maximum age was 80 years with papillary serous cystadenocarcinoma. Maximum number of cases were seen in age group from 21-30 years (28.3%), then 31-40 years (22.2%) and followed by11-21 years and 41-50 years (both 17%).

This is in accordance with studies conducted by T Bhuyanet al[15], Ashraf et al[17] as shown in Table 5.

Table: 5 Age distribution in various studies (%)

Age group (years)	T Bhuyan et al%	Ashraf et al%	Present study%
0-10	1.3%	0.47%	0.43%
11-20	7.4%	12.29%	17%
21-30	27%	30.19	28.3%
31-40	27%	22.64%	22.2%
41-50	19.5%	18.4%	17%
51-60	4%	10.38%	8.73%
61-70	5.2%	3.77%	5.67%
71-80	1.7%	1.41%	0.43%

The abdominal pain with bleeding P/V is prototype clinical presentation for most obstetric and gynecological problems. Patients presenting with these two must be properly investigated. In the present study the most common presentation for both benign and malignant tumors was abdominal pain (30.56%) followed by abnormal bleeding (26.2%). There were 15.28% of cases who presented with complaints of both pain and mass in abdomen while 13.1% presented with mass alone. The percentage of asymptomatic patients who were accidently discovered during examination or ultrasonography was 10.48% in our study. These findings were similar to researches done by Sheela KM et al[4], Kayastha et al[11], Yasmin et al[12], Akash A et al[20], Hota R et al.[21]

Usually size of an ovarian tumor is not a predictor of its nature. Some of the largest tumors can be benign. In our study the maximum number of tumors was in size range from 5-9 cm (48.47%) while most malignant tumors were greater than 10 cm in size. This was comparable to studies conducted by Hota R et al[21]. This might be due to the late presentation of patients to seek medical advice.

According to histopathological reports the most common tumor in our study was surface epithelial tumors (60.69%) followed by germ cell tumors(32.75%) and then sex cord stromal tumors(3.93%). These were in accordance to studies done by Sheela KM et al[4], Hota R et al[21] as shown in Table 6.

a) b) c)

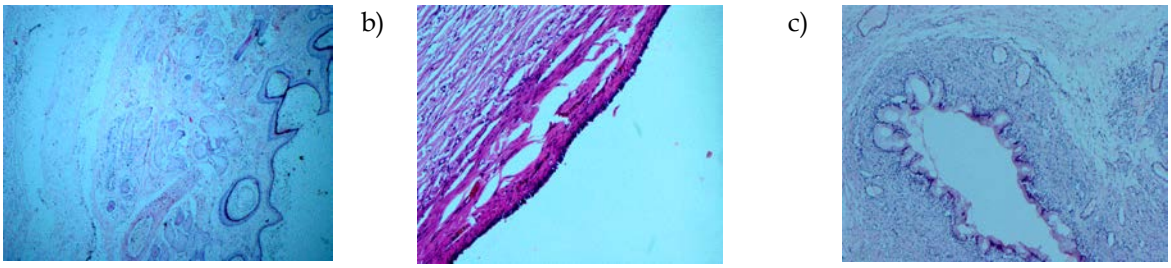

Figure: 1: Benign Tumors of ovary. a) Mature Cystic Teratoma 10x. b) Serous Cystadenoma 10x. c)Mucinous cyst adenoma 10x

a) b) c)

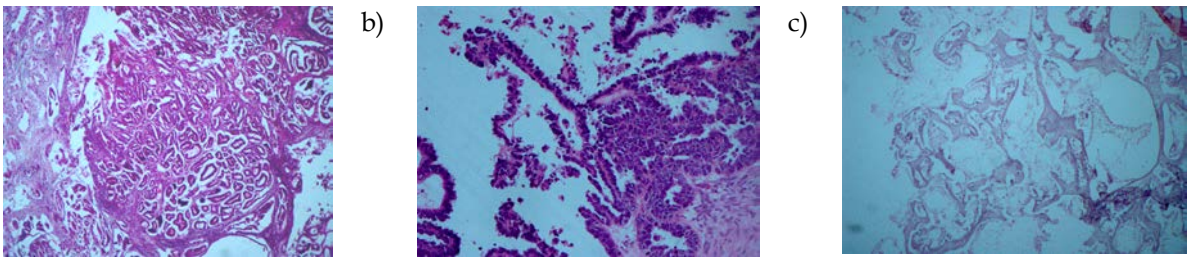

Figure 2: Malignant Tumors of Ovary. a) Endometrioid Carcinoma b)Serous Cystadenocarcinoma c)Mucinous Cystadenocarcinoma

Table:6 Comparison of Frequency of various Histopathological types of ovarian tumors %

Type of tumor	Sheela et al(n=597)	Hota R et al (n=230)	Present study (n=229)
Surface epithelial	70.3%	64.5%	60.69%
Germ cell tumor	25.5%	27%	32.75%
Sex cord stromal	4.2%	5.2%	3.93%
Poorly differentiated	0.17%	0.8%	1.74%
Metastatic	0.34%	2.6%	0.43%

In our study among benign tumors the most common was dermoid cyst (29.69%) then serous cyst adenoma (24.01%) and lastly mucinous cystadenoma (9.60%). This was in contrast to studies done by Sheela et al[4], Akash A et al[20], Hota R et al[21] and Ashraf et al[17] in which serous cyst adenoma was the most common benign tumor. In our study among the borderline tumors serous borderline tumor was more common than mucinous borderline. This was again in contrast to study done by Sheela et al[4] where mucinous borderline tumors were more common.

Among the malignant tumors the most common type in present study was serous cystadenocarcinoma (15.75%). The sex cord stromal tumors were 3.93% while endometrioid carcinomas were 3.49% and germ cell carcinoma were 3.05%. The percentage of both the mucinous cystadenocarcinoma and clear cell carcinoma was 2.62%. These findings were in comparison with studies done by Sheela et al[4], Akash et al[20], Jha& Karki[19], Hota R et al[21].

Conclusion

In our study the number of benign tumors outnumbered the malignant tumors of ovary among which the surface epithelial tumors were most frequent followed by germ cell tumors, the most common being dermoid cyst. Most patients presented with abdominal pain in the age group of 20-40 years mostly.We also noticed that the most common risk factors associated with ovarian tumors were nulliparity, menstrual irregularities, previous surgeries and a family history of ovarian/breast cancers.. Furthermore, the histological diagnosis of ovarian tumors is crucial for further management. This can be attained by collaboration of clinical, radiological and surgical pathology departments. Social awareness campaigns on media as well as through women health workers can contribute towards awareness in general public and early detection and management.

Recommendations

It is crucial to correlate history, clinical examination, morphological features and presence of various risk factors in order to arrive at an early diagnosis which is vital for lessening the mortality and improving the prognosis of ovarian tumors. . The social taboo of modesty and reluctance among our females to consult a doctor/health care worker about her medical issues is a big hurdle in getting timely diagnosis and management. Education of the masses at the primary health care level about health issues is crucial

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